## Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

### Listing of Claims:

Claim 1 (Original):    A method for determining candidates for gene deletions and additions using a model of a metabolic network associated with an organism, the model comprising a plurality of metabolic reactions defining metabolite relationships, the method comprising:

selecting a bioengineering objective for the organism;

selecting at least one cellular objective;

forming an optimization problem that couples the at least one cellular objective with the

bioengineering objective; and

solving the optimization problem to yield at least one candidate.

Claim 2 (Previously presented):    The method of claim 1 further comprising using the at least one candidate to genetically modify the organism.

Claim 3 (Original):    The method of claim 1 wherein the bioengineering objective is overproduction of a chemical.

Claim 4 (Original):    The method of claim 1 wherein the bioengineering objective is underproduction of a chemical.

Claim 5 (Original):    The method of claim 1 wherein the cellular objective is growth.

Claim 6 (Withdrawn):       The method of claim 1 wherein the cellular objective is minimization of metabolic adjustment.

Claim 7 (Original):    The method of claim 1 wherein the candidate is a candidate for gene deletion, and the optimization problem includes a binary value for specifying if reaction flux is active or inactive.

Claim 8 (Original):    The method of claim 1 wherein the optimization problem is a bilevel optimization problem.

Claim 9 (Withdrawn): The method of claim 1 wherein the optimization problem is a mixed-integer optimization problem.

Claim 10 (Original):   The method of claim 1 wherein the optimization problem includes at least one stoichiometric constraint.

Claim 11 (Original):   The method of claim 1 wherein the optimization problem includes at least one chemical uptake constraint.

Claim 12 (Original):   The method of claim 1 wherein the step of forming an optimization problem includes quantifying the cellular objective as an aggregate reaction flux.

Claim 13 (Original):   The method of claim 1 further comprising evaluating performance limits of the metabolic network with the at least one candidate based on ability of the network to meet the at least one cellular objective.

Claim 14 (Original):   The method of claim 1 wherein the cellular objective is selected from the group consisting of: maximizing a growth rate, maximizing ATP production, minimizing metabolic adjustment, minimizing nutrient uptake, minimizing redox production, minimizing a Euclidean norm, and combinations thereof.

Claim 15 (Withdrawn):       The method of claim 1 wherein the bioengineering objective is overproduction of glycerol and at least one candidate is for gene deletion and comprising genes coding for the enzymes fructose- 1,6-bisphosphatase, fructose- 1,6-bisphosphatase aldolase, phosphoglycerate kinase, glyceraldehydes-3-phosphate dehydrogenase, phosphoenolpyruvate synthase, NADH dehydrogenase I, phosphogluconate dehydratase, 2-keto-3-deoxy-6-phosphofluconate aldolase, triosphosphate isomerase, glucose 6-phosphate-1 -dehydrogenase, 6-phosphogluconolactonase- , deoxyribose-phosphate aldolase, aldehyde dehydrogenase, or combinations thereof.

Claim 16 (Withdrawn):       The method of claim 1 wherein the bioengineering objective is overproduction of 1,3-propanediol and at least one candidate is for gene deletion and comprising genes coding for the enzymes fructose- 1,6-bisphosphatase, fructose- 1,6-bisphosphatase aldolase, phosphoglycerate kinase, glyceraldehyde-3-phosphate dehyrogenase, triosphosphate isomerase,

glucose 6-phosphate-1-dehydrogenase, 6-phosphogluconolactonase, deoxyribose-phosphate

aldolase, aldehyde dehydrogenase, or combinations thereof.

Claim 17 (Withdrawn):    The method of claim 1 wherein the bioengineering objective is

overproduction of succinate and at least ape candidate is for gene deletion and comprising genes

coding for the enzymes pyruvate formate lyase, acetaldehyde dehydrogenase, pyruvate kinase,

FOF1-ATPase, NADH dehydrogenase I, fumarase, D-Lactate dehydrogenase, pyridine nucleotide

transhydrogenase, phosphotransacetylase, acetate kinase, phosphotransferase, or combinations

thereof.

Claim 18 (Original):   The method of claim 1 wherein the bioengineering objective is

overproduction of lactate and at least one candidate is for gene deletion and comprising genes

coding for the enzymes phosphotransacetylase, acetate kinase, phosphofructokinase, fructose-4

1,6-bisphosphatase aldolase, triosphosphate isomerase, acetaldehyde dehyrogenase, glucokinase,

or combinations thereof.

Claim 19 (Previously presented):    A computer-based method for determining candidates for

gene deletions and additions using a model of a metabolic network associated with an organism,

the model comprising a plurality of metabolic reactions defining metabolite relationships, the

method comprising:

inputting at least one bioengineering objective;

receiving as input as least one cellular objective;

forming an optimization problem that quantifies the cellular objective as an aggregate reaction

flux and couples the at least one cellular objective with the bioengineering objective;

solving the optimization problem to yield at least one candidate; and outputting the at least one

candidate.


Claim 20 (Previously presented):    The method of claim 1 wherein the cellular objective

comprises maximizing a growth rate.